b. autoclaving the mixture from said step a until RNA is completely digested;

c. cooling the product from said step b, said cooled product comprising solids;

d. removing said solids from the product from said step c;

e. adding water to the product from said step d; and

f. adjusting the pH of the product from said step e to a biological acceptable pH range.

REMARKS

This is responsive to the Office Action dated March 23, 2001. Reconsideration is respectfully requested in view of the above amendment and the following remarks.

Claims 1 and 7 have been further amended.

Claims 1-4 and 7-9 are now pending.

The previous amendment to the description of the invention has been canceled without prejudice.

Objection under 35 U.S.C. 132

The examiner objects to applicants' previous amendment to the description of the invention under 35 U.S.C. 132 on the ground that the incorporation by reference of U.S. patent application Serial No. 09/344,095, which discloses Product R's physical and chemical properties is new matter because that application was filed subsequent to the instant application. However, U.S. patent application Serial No. 09/344,095 was a continuation in part (CIP) of U.S. patent application Serial No. 08/735,236, filed on October 22, 1996, more than two years prior to the filing date of the instant application. The process of making Product R was fully disclosed in the

parent application. Although Product R's physical and chemical properties was unknown at the time when the parent application was filed in 1996, they are inherent properties of the product, which has been in existence at least since the filing dated of that parent application. Therefore, applicants respectfully disagree with the Examiner in that Product R's physical and chemical properties are new matter.

Notwithstanding applicants' disagreement with the Examiner, applicants have canceled the previous amendment to the description of the invention. It is respectfully requested that the Examiner's objection to new matter should be withdrawn.

Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejects claims 1-4 and 7-9 under 35 U.S.C. 112, first paragraph, on the ground that applicants described two methods of making Product R but did not provide any proof that these two methods result in the same product. The Examiner further suggests that this rejection may be overcome by amending the claim to include a specific method of preparing Product R intended to be encompassed by the claims. Applicants have amended the claims 1 and 7, the independent claims, in accordance with the Examiner's suggestion. It is respectfully submitted that rejection to claims 1-4 and 7-9 under 35 U.S.C. 112, first paragraph, has been overcome and should be withdrawn.

Rejection under 35 U.S.C. 112, second paragraph

The Examiner rejects claims 1-4 and 7-9, under 35 U.S.C. 112, second paragraph, as being vague and indefinite with respect to "the amount of said RT-PCT product to determine the reduction of said RT-PCR product". Responsive to the Examiner's rejection, applicants have amended the claim languages to clarify how the measurement of down-regulation of gene

expression of HIV coreceptor is conducted, which are shown in the above amendment of the claims.

Specifically, the claim languages are amended to indicate that progressively increasing amounts of Product R are introduced into different groups of the cells such that the cells treated with different amount of Product R will produce different amount of HIV coreceptor gene product (RT-PCR product), i.e., the cells treated with more Product R result in less gene expression product (RT-PCR product). Comparison of the relative amounts of RT-PCR product resulting from those different treatments demonstrates down regulation of the gene by Product R.

Measurement of a RT-PCR product can be achieved by any conventional methods, such as electrophoresis, dot-blotting, or scintillation, which are well known to a person of ordinary skill in the art.

Accordingly, the rejection to claims 1-4 and 7-9 has been overcome and should be withdrawn.

Allowance of claims 1-4 and 7-9 is respectfully requested.

This preliminary amendment is presented to place the application in better form for allowance. No new matter has been added. Early examination and favorable consideration of the above-identified application is earnestly solicited.

Any additional fees or charges required at this time in connection with the application may be charged to our Patent and Trademark Office Deposit Account No. 03-2412.

Respectfully submitted,
COHEN, PONTANI, LIEBERMAN & PAVANE

By: _____

Yunling Ren
Reg. No. 47,019
551 Fifth Avenue, Suite 1210
New York, N.Y. 10176
(212) 687-2770

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION:

Page 4, change the paragraph beginning on line 15 as follows:

Product R (RETICULOSE) is a synthesized preparation that contains a mixture of peptide nucleic acids, breakdown components of bovine serum albumin, and, probably, free nucleosides. Although little is known about the chemical nature of Product R, its biological activities have been demonstrated in effective treatment of influenza in the 1930's, in stimulation of growth of bone marrow cells and granulocytes in rabbits post-irradiation in the 1950's, and significant improvement of life quality and immunologic profile of AIDS patients in a most recent clinical trial. To understand Product R-mediated immunoregulatory activities, Chen and Hirschman have made efforts in testing its biological effect on the production of cytokines by HI V-infected human T cell lines and primary peripheral blood mononuclear cells (PBMCs). *J. Investig. Med 1996; 44:347-351.* Their primary finding clearly demonstrated that [Reticulose] Product R potentiated the production of IFN-gamma and IL-6 as well as inhibited HIV replication in PBMCs.

IN THE CLAIMS:

Please amend claims 1 and 7 as follows:

1. (Twice Amended) A method for determining down-regulation of gene expression of a human immunodeficiency virus (HIV) coreceptor, comprising the steps of:

a. culturing cells capable of expressing said human HIV coreceptor;

b. dividing said cultured cells into a plurality of groups;

c [b]. introducing predetermined progressively increasing amounts of Product R to said plurality of groups of said cultured cells, respectively, by electroporation;

d [c]. culturing said plurality of groups of said electroporated cells;

e [d]. preparing a total RNA from each said group of said cultured electroporated cells after step d [c], respectively;

f [e]. reverse-transcribing the mRNA of said HIV coreceptor from each said total RNA by a reverse transcription-polymerase chain reaction [(RT-PCT)] (RT-PCR) to produce an RT-PCR product [of the gene expression of said HIV coreceptor]; [and]

g [f]. measuring the amount of said RT-PCR product produced from each said group of said cells [to determine the reduction of said RT-PCR product.] ; and

h. comparing the relative amounts of said RT-PCR products from said plurality of groups of said cells to determine the reduction of said RT-PCR product,

wherein Product R is made by a process comprising the steps of:

g. mixing predetermined amounts of casein, beef peptone, ribonucleic acid (RNA), bovine serum albumin and sodium hydroxide in a predetermined amount of water;

h. autoclaving the mixture from said step a until RNA is completely digested;

i. cooling the product from said step c, said cooled product comprising solids;

j. removing said solids from the product from said step c;

k. adding water to the product from said step d; and

l. adjusting the pH of the product from said step e to a biological acceptable pH range.

7. (Amended) A method for determining down-regulation of gene expression of a human immunodeficiency virus (HIV) coreceptor, comprising the steps of:

a. dividing cells capable of expressing said human HIV coreceptor into a plurality of groups;

b [a]. [electroporating cells to introduce] introducing predetermined progressively increasing amounts of Product R into said plurality of groups of said cells [capable of expressing said human HIV coreceptor], respectively, by electroporation;

c [b]. reverse-transcribing the mRNA of said HIV coreceptor of each said groups of said cells by a reverse transcription-polymerase chain reaction [(RT-PCT)] (RT-PCR) to produce an RT-PCR product [of the gene expression of said HIV coreceptor]; [and]

d [c]. measuring the amount of said RT-PCR product produced from each said group of said cells [to determine the reduction of said RT-PCR product.]; and

e. comparing the relative amounts of said RT-PCR products from said plurality of groups of said cells to determine the reduction of said RT-PCR product,

wherein Product R is made by a process comprising the steps of:

a. mixing a predetermined amounts of casein, beef peptone, ribonucleic acid (RNA), bovine serum albumin and sodium hydroxide in a predetermined amount of water;

b. autoclaving the mixture from said step a until RNA is completely digested;

c. cooling the product from said step b, said cooled product comprising solids;

d. removing said solids from the product from said step c;

e. adding water to the product from said step d; and

f. adjusting the pH of the product from said step e to a biological acceptable pH range.